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Diagnosis of sarcopenia with magnetic resonance imaging of newly diagnosed pediatric inflammatory bowel disease

Sarcopenia in pediatric inflammatory bowel disease

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Abstract

Aim: Patients with inflammatory bowel disease (IBD) are at a high risk of sarcopenia. This study aimed to evaluate sarcopenia by estimating muscle mass with magnetic resonance imaging of newly diagnosed IBD.

Material and Methods: Pediatric IBD patients, who underwent magnetic resonance enterography (MRE) from 2019 to 2022, were enrolled. Demographic, anthropometric, laboratory and clinical data were retrospectively obtained from medical records. The total Psoas Muscle Area (tPMA) and Skeletal Muscle Area (SMA) were calculated by scanning the psoas muscle areas at the upper level of the L4 vertebra and all muscle areas in the same section on axial T2-weighted images. Sarcopenia diagnosis was made according to Pediatric Reference Analytic Morphomics Population (PRAMP) growth charts.

Results: We enrolled 26 IBD patients, 11 (42.3%) with Crohn's disease (CD) and 15 (57.7%) with ulcerative colitis (UC) (median age 15, IQR=4.25 years). Among patients, 14 (54%) cases had sarcopenia. IBD patients treated with biologics had a lower tPMA index (p=0.036) than those treated with 5-ASA and steroids. tPMA and tPMA indexes were significantly lower in the group with vitamin D levels below 20 ng/ml (p=0.018, p=0.015, respectively). A significant correlation was also found between the tPMA index and serum vitamin D levels (r=0.429, p=0.029).

Discussion: This study demonstrated a high prevalence of sarcopenia with 54% and lower SMA in newly diagnosed pediatric IBD patients. Muscle mass measurement in MRE studies highlighted that sarcopenia should be considered in vitamin D deficiency and in the case of normal anthropometric measurements.

Keywords

Sarcopenia, Child, Inflammatory Bowel Disease, Skeletal Muscle Mass, Magnetic Resonance Enterography

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Introduction

The importance of sarcopenia in inflammatory bowel disease (IBD) is beginning to be recognized in the pediatric age. Crohn's disease (CD) and ulcerative colitis (UC) are chronic disorders and growth failure is one of the most frequent extraintestinal manifestations of pediatric onset disease. Undernutrition was observed in 14.3% of pediatric IBD patients and 16% of adult patients with IBD suffer from malnutrition which has serious consequences for IBD [1,2]. It has been reported that 22–24% of children with CD and 7–9% of children with UC had low BMI [3]. In clinical practice, basic anthropometric measurements such as body mass index (BMI) are routinely used to assess growth. Generally, the methods used for the evaluation of nutritional status, are not accurate enough to estimate body composition, which may differ between healthy individuals and patients with IBD. A pediatric systematic review documented lean mass deficits in 93.6% of CD and 47.7% of UC compared with healthy controls [4]. The skeletal muscle mass (SMM) can be measured by several radiological methodologies including whole-body dual X-ray absorptiometry (DXA), computed tomography (CT), magnetic resonance (MR), ultrasound (US) and peripheral quantitative CT [4,5]. Age and gender-specific psoas muscle area (PMA) percentile curves obtained from CT images of healthy children, were recently modeled in pediatric studies [6,7]. Total cross-sectional muscle area of the abdominal wall was also evaluated and recorded as Skeletal Muscle Area (SMA) in a study using MRE images of adults with CD [8].

Loss of SMM and reduced muscle strength or physical performance is named sarcopenia by the European Working Group on Sarcopenia in Older People (EWGSOP2), and it is considered an important component of malnutrition [9]. While sarcopenia is mainly observed in older people, it can also develop at a younger age as a manifestation of IBD [10]. Beyond the description, sarcopenia is almost identical to frailty, a clinical syndrome that reflects increased vulnerability to medical stressors, which indicates additional dimensions of health, not captured by standard laboratory measures [10]. However, pediatric sarcopenia is a very new subject and there are many unknowns. The role of sarcopenia in IBD is still unclear in childhood. Considering all these, we need basic tools to evaluate the body composition of children with IBD in clinical practice such as CT or MR data that have already been done in routine assessment.

Thus, we aimed to compare SMA and total Psoas Muscle Area (tPMA) of pediatric IBD patients and controls, to evaluate and investigate the relationship of sarcopenia with clinical features, laboratory findings, medical treatments and clinical outcomes of the patients.

Material and Methods

Ethical Consideration

This study was approved on 2022-11-24 by the Local Ethics Committee of the University (#2022/24-11) and was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from all subjects involved in the study.

Participants

This case-control study was conducted in a tertiary care children's hospital between January 1, 2019, and January 1, 2022. Pediatric IBD patients (<18 years of age) who were followed up for at least one year at the Pediatric Gastroenterology outpatient clinic and underwent MRE at the time of initial diagnosis were included. IBD was diagnosed according to the European Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) revised Porto criteria for the diagnosis of IBD in children and adolescents [11]. The control group included children of a similar age who had no chronic disease and underwent an MR imaging (MRI) study of the abdominal or lumbar spine. Children with missing data, any abnormal imaging findings, or low-quality MRE or MRI studies were excluded. Children with any other chronic diseases such as malignancy, chronic inflammatory diseases, acute or chronic infection, genetic diseases, or significant anatomic deformity were excluded. None of the patients or controls were professionally involved in sports.

Study Design

Demographic characteristics, anthropometric measurements, laboratory and clinical data, medications, disease activity, disease exacerbations in children with IBD were retrospectively obtained from medical records. Disease activity was assessed by the Pediatric Crohn's Disease Activity Index (PCDAI) and the Pediatric Ulcerative Colitis Activity Index (PUCAI) [12,13]. Disease exacerbation was defined as the relapse of clinical symptoms after disease remission, accompanied by an elevation of the PCDAI or PUCAI above 10 points. As for the control group, data including age, sex, height, and weight at the time of the MRI were recorded.

Muscle Mass Measurement

A gastroenterologist, who was blinded to the patient's name and clinical data, analyzed and measured each PMA by scanning the right and left psoas muscle areas at the upper level of the L4 vertebra demonstrated on MRI by a freehand region of interest (ROI) using PACS GE Healthcare, and the sum of the two muscles were recorded as tPMA. Skeletal Muscle Area (SMA) was recorded by scanning the total cross-sectional muscle area of the abdominal wall at the same level using the same tool enabling the exclusion of the vertebra. The tPMA and SMA divided by the body surface area yielded the tPMA and SMA index. The tPMA was assessed also with age and gender-specific Pediatric Reference Analytic Morphomics Population (PRAMP) charts that are calculated by CT scans divided into quantiles for further analysis of the study population [7]. Sarcopenia was defined as a measurement under the 5th quantile according to PRAMP growth charts evaluating tPMA at L4, specific for age and gender [7].

Statistical Analysis

Continuous variables were presented as mean and standard deviation (SD), median and interquartile range (IQR) based on distribution evaluated by Shapiro-Wilk test. The categorical data were presented as a number of cases and percentages. Normally distributed and skewed variables of two different groups were compared by Student's t-test and Mann- Whitney U test, respectively. The x^2 test or Fisher's exact test was performed to compare categorical variables in different groups. Correlations between variables in patients with IBD were evaluated by Spearman's correlation analysis. The Statistical Package for the

Social Sciences (SPSS) 22.0 (IBM Corp, Armonk, NY) was used for all statistical analyses, and a p-value <0.05 was considered statistically significant.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

Twenty-six IBD patients, including 15 (57.7%) UC and 11 (42.3%) CD were enrolled, and 22 children were included in the control group. Samples of muscle measurements are shown in Figure 1.

A comparison of demographic, anthropometric, and laboratory data of the patients with the control group is presented in Table 1. Considering the anthropometric data of patients with IBD, a significant positive correlation was found between the median height Z score and tPMA (r=0.422, p=0.032), but there were no correlations between tPMA and BMI, weight Z score (r=0.287, p=0.156 and r=0.376, p=0.059, respectively).

Table 1. Demographic, anthropometric and laboratory features of the study population and controls.

		IBD n=26	Controls n=22	p value
Age (years) median (IQR)		15.00 (4.25)	15.00 (3.25)	0.958
Gender, n (%)	Boys	15 (57.7)	9 (40.9)	0.247
	Girls	11 (42.3)	13 (59.1)	
Z score of body mass index +		-1.72 ± 2.05	-0.19 ± 1.46	0.005
Z score of weight+		-1.49 ± 1.56	-0.32 ± 1.40	0.010
Z score of height+		-0.27 ± 1.14	-0.24 ± 1.19	0.942
Body surface area (m^2)		1.37 ± 0.27	1.52 ± 0.23	0.037
Total psoas area (mm^2)		1404.6 ± 522.1	1668.3 ± 699.8	0.142
Total psoas area index		1019.6 ± 316.0	1078.2 ± 377.2	0.561
Skeletal muscle area (mm^2)		7828.5 ± 2009.6	9459.0 ± 2781.3	0.023
Skeletal muscle area index		5723.5 ± 1197.1	6125.3 ± 1259.0	0.264
Serum protein (g/dL) mean ± SD		6.66 ± 0.74	7.24 ± 0.43	0.002
Serum albumin (g/dL) mean ± SD		3.56 ± 0.65	4.28 ± 0.29	<0.001
C-reactive protein median (mg/L) (IQR)		3.0 (7.4)	0.29 (0.50)	<0.001
Erythrocyte sedimentation rate (mm/hr) median (IQR)		47.9 (24.5)	13.0 (10.5)	<0.001

+ According to 2006 National Growth Charts (Neyzi O, Furman A, Bundak R, Gunoz H, Darendeliler F, Bas F. Growth references for Turkish children aged 6 to 18 years. Acta Paediatr. 2006; 95:1635-41)

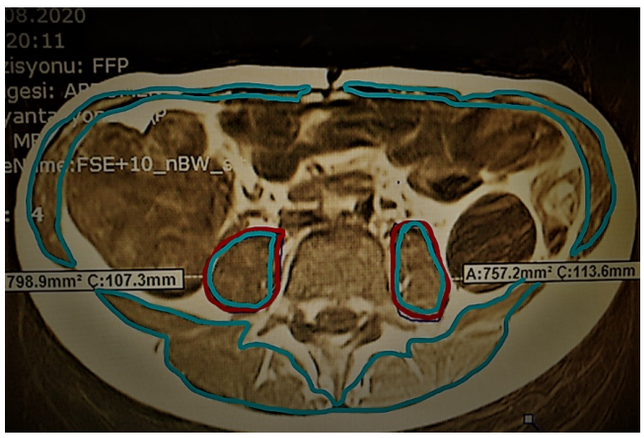

Figure 1. Description of muscle mass measurements (areas outlined in red indicate total Psoas Muscle Area, areas outlined in blue indicate Skeletal Muscle Area).

Additionally, no correlation was found between the median height Z score and SMA (r=0.368, p=0.064), while a significant correlation was found between the BMI, weight Z score and SMA (r=0.461, p=0.018 and r=0.545, p=0.004 respectively). When the muscle mass measurements of groups based on laboratory and radiological findings of patients with IBD were compared, only tPMA and tPMA indexes were significantly lower in the group with serum Vitamin D levels below 20 ng/ml (p=0.018, P=0.015, respectively). Regarding laboratory findings, a significant correlation was found between the tPMA

Table 2. Therapy, clinical outcome, and muscle mass measurements of IBD patients.

	tPMA (mm^2) median (IQR)	tPMA index median (IQR)	SMA (mm^2) median (IQR)	SMA index median (IQR)
Enteral nutrition				
Administered, n=20	1294.0 (601.0)	1014.8 (510.4)	7007.0 (3039.0)	55472.5 (2493.6)
Not administered, n=6	1622.5 (957.7)	1055.2 (646.9)	9301.5 (2387.7)	6869.4 (1042.6)
p-value	0.201	0.543	0.024	0.301
5-Aminosalicylic acid				
Administered, n=23	1406.0 (697.0)	1060.3 (515.5)	8077.0 (2956.0)	5952.4 (1920.3)
Not administered, n=3	967.0 (-)	727.9 (-)	5707.0 (-)	4206.4 (-)
p-value	0.071	0.033	0.049	0.022
Corticosteroids				
Administered, n=22	1455.5 (757.7)	1071.5 (535.9)	8231.0 (3210.2)	6041.3 (2025.7)
Not administered, n=4	1084.0 (559.5)	753.8 (368.1)	6403.5 (2313.2)	4254.7 (1142.7)
p-value	0.118	0.047	0.088	0.039
Corticosteroid response				
Responsive, n=13	1336.0 (688.5)	1082.7 (445.3)	6130.1(2364.6)	8077.0 (3298.5)
Addicted/ Resistant, n=13	1375.0 (837.5)	869.8 (478.4)	5967 (2217.5)	6908.0 (2997.5)
p value	0.858	0.054	0.086	0.427
Immunomodulators				
Administered, n=22	1455.5 (760.5)	1060.9 (520.0)	8231.0 (3669.7)	6041.3 (2236.4)
Not administered, n=4	1268.5 (749.2)	880.9 (535.5)	6919.5 (2716.5)	4825.7 (1632.4)
p-value	0.543	0.394	0.181	0.100
Biologics				
Administered, n=13	1375 (808.0)	869.8 (521.1)	8077.0 (3086.0)	5596.7 (2302.8)
Not administered, n=13	1336.0 (940.0)	1082.7 (583.5)	6908.0 (3116.0)	6130.1 (2378.8)
p-value	0.622	0.036	0.421	0.102
Ileal involvement				
Present, n=19	1258.0 (1137.0)	990.5 (666.4)	6893.0 (3653.0)	4958.9 (2014.4)
Absent, n=7	1375.0 (441.0)	1039.1 (493.9)	7836.0 (2565.0)	5895.6 (2243.9)
p-value	0.665	0.751	0.538	0.665
Perianal disease				
Present, n=5	967.0 (1539.0)	779.8 (882.0)	9653.0 (5902.5)	6435.3 (2779.5)
Absent, n=21	1375.0 (414.0)	1039.1 (463.6)	7348.0 (2649.0)	5597.1 (2090.5)
p-value	0.537	0.820	0.974	0.974
Disease activity				
Mild, n= 6	1381.5 (671.2)	1036.6 (444.4)	6553.0 (1936.0)	5455.7 (2532.0)
Moderate/severe, n= 20	1355.5 (879.2)	1010.6 (618.2)	8231.0 (3282.0)	5746.4 (2532.1)
p-value	0.503	0.903	0.100	0.951

tPMA=total psoas muscle area; SMA=skeletal muscle area

Table 3. Demographic, laboratory features and muscle mass measurements of the IBD-diagnosed patients with and without sarcopenia.

		*Sarcopenic IBD patients, n =14	*Non-sarcopenic IBD patients n=12	p value
Age (years) median (IQR)		15.5 (2.25)	13.00 (5,75)	0.021
Gender, n (%)	Boys	9 (64.3)	6 (50.0)	0.462
	Girls	5 (35.7)	6 (50.0)	
SMA (mm^2) median (IQR)		6996.5 (4069.8)	8231.0 (2578.3)	0.198
SMA index median (IQR)		5455.7 (2461.9)	5746.4 (1558.9)	0.504
Z score of BMI+ median (IQR)		-2.2 (2,8)	-1.3 (1.9)	0,076
Z score of weight+ median (IQR)		-2.2 (2.2)	-0.7 (2,6)	0.017
Z score of height+ median (IQR)		-0.8 (1.3)	0.3 (1.5)	0.017
Body surface area (m^2) median (IQR)		1.4 (0.3)	1.4 (0.3)	0.280
Serum albumin (g/dL) median (IQR)		3.5 (0.9)	3.8 (0.9)	0.320
Serum Vitamin D (ng/ml) median (IQR)		14.0 (13.2)	14.5 (11.7)	0.690
C-reactive protein (mg/L) median (IQR)		5.8 (7.8)	1.4 (2.9)	0.048
Erythrocyte sedimentation rate (mm/hr) median (IQR)		58.0 (21.3)	44.0 (11.5)	0.035

*Sarcopenia was defined as a measurement under the 5th quantile according to PRAMP growth charts evaluating tPMA at L4 specific on age and gender [10] + According to 2006 national growth charts [38]. SMA= skeletal muscle area; BMI= body mass index

index and serum vitamin D levels (r=0.429, p=0.029), while there was no correlation with the other muscle area measurements. Additionally, it was seen that vitamin D levels correlated with serum albumin levels in the IBD patients (r=0.389, p=0.049).

In terms of treatment and clinical outcome, IBD patients treated with biologics had lower tPMA index, compared with data of patients treated with 5-ASA and steroids. As a similar finding, 5-ASA and steroid users had higher SMA indexes compared to non-users (Table 2).

Among patients with IBD, 14 (54%) cases had sarcopenia according to PRAMP growth charts [7]. The demographic, anthropometric, and laboratory features of the patients with and without sarcopenia are presented in Table 3. Patients with low albumin levels (under 3.5 g/dL), pANCA positivity, anal disease, terminal ileal involvement, response to steroid, and need to use the biologics was similar in sarcopenic and non-sarcopenic IBD patients (p=0.671, 0.126, 0.330, 0.275, NS, 0.951, respectively).

Discussion

This is one of a limited number of studies evaluating sarcopenia in pediatric IBD. We emphasized a high ratio of sarcopenia with 54% in our study population. SMA was significantly lower in the IBD group than in controls, while other muscle mass parameters were similar. Patients with a vitamin D level under 20 ng/ml had lower tPMA and tPMA index. When we approached treatment data, IBD patients who were administered enteral nutrition had significantly lower SMA values and patients who had to use biological treatment had significantly lower tPMA index. We indicated that the patients with sarcopenia were older than non-sarcopenic patients. Contrary to reports showing that sarcopenia correlates with the severity of IBD, none of our study's muscle mass measurements differed according to disease activity [14,15].

There is still no standard radiological measurement for evaluating muscle mass. The tPMA and SMA have been increasingly applied as markers of sarcopenia in IBD patients [14,16]. In more than half of the reports, CT is used to assess sarcopenia, but MRI has the greatest ability to differentiate muscles from surrounding tissues, rather than a CT scan for assessment of muscle volume [17,18]. MRI is routinely used in pediatric IBD to assess small bowel inflammation, alongside assessment of stricturing and fistulating disease [12]. Routine MRI scans can be useful in assessing lean muscle mass in children with IBD and help choose optimized nutritional support. In this study, we underlined the usefulness of MRI images for the evaluation of muscle mass in pediatric IBD. Also, our study showed that sarcopenic and nonsarcopenic IBD patients had similar Z scores of BMI. This result shows us the need for advanced methods to evaluate sarcopenia other than standard anthropometric parameters.

We indicated that the patients with sarcopenia were older than non-sarcopenic patients. In a pediatric study, the fat-free mass increased over 10 years from 5 years before peak height velocity to 5 years after peak height velocity [19]. The increase in muscle mass during adolescence is very rapid and probably more severely affected by growth failure and undernutrition in patients with IBD.

Chronic inflammation plays a big role in the development of sarcopenia in IBD. Inflammatory cytokines are associated with reduced muscle protein synthesis. Serum inflammatory markers, such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), are typically elevated in active disease and are sensitive in the diagnosis of new-onset IBD patients [16]. In our results, IBD diagnosed group with sarcopenia had significantly higher CRP and ESR compared to the non-sarcopenic group in contrast to Mager et al [20] data.

In a pediatric UC study, 62% of patients were reported to have sarcopenia [17]. In another study of pediatric IBD, 31% of CD and 14.8% of UC were defined as sarcopenic [21]. Similarly, 54% of our IBD patients had sarcopenia according to the PRAMP charts (tPMA measured under the 5th quantile for L4 psoas muscle area) [7].

It was reported that the presence of sarcopenia has prognostic effects in patients with IBD [23]. Treatment choices, such as enteral nutrition, biologics, and steroids change the nutritional status of IBD patients. We showed that the detection of sarcopenia at diagnosis is more likely to require the use of biological therapy. Our results were supported by the study by Atlan et al, which reported a relationship between sarcopenia and biological therapy, and disease exacerbation in pediatric age [14]. This study has highlighted that there was no difference in the muscle areas of patients responsive and non-responsive to steroids besides the higher tPMA and SMA indexes in steroid users. In children with IBD, corticosteroids are the first choice for inducing remission, and biologics are recommended for patients with a high risk for a complicated disease course. Concerning this, patients under treatment with steroids had higher tPMA and SMA indexes. Despite we evaluated muscle mass parameters at diagnosis, it can be speculated that biologics would be the first choice of treatment in newly diagnosed patients with sarcopenia to improve muscle mass. In an adult study, it was demonstrated that Infliximab improves both muscle mass and muscle strength in patients with CD [23].

On the other hand, administration of corticosteroids causes muscular atrophy [24].

There is a lack of studies investigating the vitamin D status and concurrent skeletal muscle mass of pediatric IBD. Mager et al. demonstrated that sarcopenia is related to vitamin D deficiency in newly diagnosed younger children with CD [20]. Another study reported lower serum levels of vitamin D in children with IBD compared to controls with no correlation to bone mineral density [25]. Our study detected lower tPMA and tPMA index in the IBD group with serum Vitamin D levels below 20 ng/ml and, to our knowledge, is the first one showing a significant correlation between vitamin D deficiency and tPMA index in pediatric IBD patients.

Limitations

The fact that there are few studies on sarcopenia in pediatric IBD patients adds to the value to our study as well, but there are also limitations. One of them is the small sample size, and the other is the absence of national, age- and gender-specific pediatric muscle mass percentile curves, which would have given a more reliable result to predict sarcopenia. Additionally, no information about muscle strength/functionality was available. In addition, the follow-up of the change in muscle mass after treatments would have contributed to the article.

Conclusion

In summary, pediatric newly diagnosed IBD had a high sarcopenia prevalence of 54% and lower SMA. This study has highlighted that sarcopenia should be considered in vitamin D deficiency and in case of normal BMI. Sarcopenia was related to higher age at diagnosis and higher levels of CRP and ESR. tPMA and tPMA index were lower in patients with low vitamin D levels. IBD patients treated with biologics had a lower tPMA index than those who did not. Further prospective studies are needed to examine factors influencing sarcopenia risk and sarcopenia effects on outcomes in larger pediatric IBD groups of patients.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of Interest

The authors declare no conflict of interest.

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